REMARKS

Claims 1-13 are pending in the subject application. The undersigned wishes to thank Examiner Michael for granting a telephonic interview on August 2, 2005. Examiner Szperka indicated in the interview that he had not entered the communication filed by applicants on July 1, 2005 because he objected to the submission of the reference "Veldman *et al.* (2004) *J. Immunol.*; 172(10): 6468-75" contained therein as Exhibit B. In response, applicants submit this communication which does not contain the objected reference. Entry of this amendment is respectfully requested.

Specification

Applicants acknowledge that the Examiner has withdraw the rejections to the specification based on applicant's submission of a substitute specification.

Oath/Declaration

The Examiner objects to the declaration as allegedly failing to comply with 37 CFR 1.67(a). Specifically, the Examiner alleges (a) that the declaration fails to identify the application by its serial number and (b) that it contains an alteration (to the address of one inventor) that is not initialed and dated. In response, applicants submit a newly executed declaration correcting these alleged deficiencies. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim Rejections under 35 USC 112 1st Paragraph-Written Description

Applicants acknowledge the Examiner's admission that the claims comply with the written description requirement of 35 USC 112 1st paragraph.

Claim Rejections under 35 USC 112 1st Paragraph-Enablement

The Office Action maintains its rejection of claims 1-11, and further rejects new claims 12 and 13, under 35 USC 112 1st paragraph, as allegedly failing to comply with the enablement requirement.

The Office Action concedes that the specification fully enables how to make the claimed compositions and peptides, but alleges that the specification does not provide sufficient enablement for using the claimed peptides and compositions.

In the previous Office Action, Applicants set forth at least three uses of the claimed peptides that were enabled by the specification:

(i) the use of the peptides to generate animal models of autoimmune disease though immunization with the peptides (page 52, lines 4-10);

(ii) the administration of the peptide at high doses to induce high dose tolerance, with specific reference to WO94/06828 (page 52, line 15 to page 53, line 19);

(iii) the vaccination of a subject against a human pathogen implicated in the etiology of a human autoimmune disease such as pemphigus vulgaris (page 53, line 20 to page 56 line 4).

The Examiner alleges these three uses occur *in vivo*, and that they "have the common theme that recognition of the claimed desmoglein 3 peptide sequence (SEQ ID NO:1) by cells of the immune system causes or lessens the severity (through the process of tolerance) of the autoimmune disease pemphigus vulgaris (PV)." The Examiner further alleges that Veldman demonstrates T cell recognition of an epitope corresponding to SEQ ID NO:1 in PV patients and healthy controls, allegedly indicating that recognition of this epitope is not causative or therapeutic for PV.

Based on this interpretation of Veldman, the Examiner alleges that a skilled artisan would not know how to use the peptide of SEQ ID NO:1 in applicant's enclosed embodiments since these embodiments "require that SEQ ID NO:1 be a causative or therapeutic agent for PV, yet Veldman et al. specifically state at the end of their abstract that recognition of a distinct desmoglein 3 peptides (one of which is essentially equivalent to SEQ ID NO:1) by T cells is independent from the development of PV."

Applicants traverse the Examiner rejection on each of the following independent grounds:

(I) The Office Action Fails to Consider Each of the Recited Uses of the Peptides

Applicants assert that the Office Action is considering the enablement of an alleged common feature of the three recited uses, rather than considering the enablement of the each of the three uses themselves. Therefore, the Office Action fails to consider the uses that are specifically recited in the specification in determining if at least one use is enabled, The Examiner instead focuses on the enablement of a broader, generalized feature that is allegedly common to the three uses: the Examiner focuses on the "the common theme that recognition of the claimed desmoglein 3 peptide sequence (SEQ ID NO:1) by cells of the immune system causes or lessens the severity (through the process of tolerance) of the autoimmune disease pemphigus vulgaris (PV)."

Applicants submit that uses (i) and (ii) do not recite PV. Accordingly, the Examiner is not assessing the enablement of the uses specifically recited in the specification. For example, the Office Action is completely silent as to why the invention is not enabled for use (ii) recited above, *i.e.* the administration of the peptide at high doses to induce high dose tolerance. Applicants submit that the induction of tolerance to peptides by immunization at high dosages with the peptides was well-known in the art at the time the invention was filed, as evidence by International PCT publication WO94/06828, referenced on page 52, line 17 of the originally-filed specification. Applicants respectfully note that this use does not require that the peptide necessarily be effective in treating PV. The peptide can merely be used to induce tolerance to one or more of its epitopes.

Applicants respectfully remind the Examiner that MPEP 2164.01 requires that "when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use" (emphasis added). Applicants submit that the use of the claimed peptides for inducing high-dose tolerance to the epitopes on the peptides, as well as the other uses recited in the specification, correlate with the entire scope of the claims and therefore this use is sufficient to preclude a rejection for nonenablement. Furthermore, as stated above, MPEP 2164.01 requires the Examiner to consider "any enabled use" rather than trying to extract an alleged common feature of multiple uses in which to solely base the inquiry of enablement.

(II) The Peptides Taught by Veldman are Different from the Claimed Peptides

The Office Action asserts that because Veldman allegedly teaches that both healthy and PV patients have reactive T-cells to the claimed peptide, that recognition of this epitope is not causative or therapeutic for PV.

Applicants respectfully traverse, because none of the peptides used in Veldman are identical to the claimed peptide. The least divergent peptide in Veldman spans residues 189-205 of desmoglein 3, while the claimed peptide spans residues 186-204. The two peptides are not the same peptide. In fact, they share only 84% (16/19 residues) amino acid identity. Accordingly, the teachings of Veldman do not apply to the claimed peptide because they describe different peptides. Furthermore, the Office Action has failed to provide a rationale why the alleged teachings of one Desmoglein 3 peptide apply to different Desmoglein 3 peptides. The Office Action has failed to justify its underlying assumption that two peptides having 84% identity must have identical biological properties *in vivo*. Since the peptides of Veldman are different from the claimed peptide, Veldman fails to undermine the therapeutic effectiveness the properties of the claimed peptide. Should the this rejection be maintained in a future Office Communication, applicants respectfully request that the basis for this assumption be made of record so that prosecution of the application can move forward.

(III) The Logic in the Rejection is Flawed: it Confuses Necessity with Sufficiency

Even if the different peptides taught by Veldman were the same as the claimed peptide, which applicants do not concede, Veldman fails to teach or suggest that the peptides of the invention would be ineffective in treating PV. In its logic, the Office Action confuses the *necessity* of Th1 cell responses to a Dsg3 antigen with the *sufficiency* of such responses in causing PV. The Office Action reasons that if Th1 cell responses to Dsg3 are not sufficient to cause PV (and they are allegedly not sufficient because healthy subjects having those Th1 cell responses do not have PV), then the Th1 responses must play no role in causing PV. This is clearly wrong. Just because they might not sufficient, on their own, to cause PV, it does not mean that they are not a necessary and integral requirement for developing PV.

The Office Action's logic is equivalent to saying that because patients suffering from an autoimmune disease and normal subjects both have an immune system, then the immune system

cannot contribute to the autoimmune disease, or equivalent to saying that because patients suffering from an autoimmune diseases and normal subjects both have an immune system, suppressing the immune system cannot be therapeutic to the autoimmune-disease patient. Both of these statements are clearly wrong, as autoimmune diseases are caused by a malfunctioning immune system and suppression of the immune system is used to treat autoimmune diseases.

The last sentence in the abstract of Veldman, contrary to the allegation in the Office Action, only refers to the finding that the types of Dsg3 peptides that are recognized by T-cells do not change as the severity of PV progresses. The last sentence of the abstract states as follows: "these findings demonstrate that T cell recognition of distinct Dsg3 peptides is restricted by distinct HLA class II molecules and is independent from the development of Pemphigus vulgaris." The authors in Veldman found no evidence of certain peptides being associated primarily with mild PV while other peptides with severe PV, and this statement reflects this finding. This finding contrasts with other diseases where epitopes change during the course of the disease in a phenomenon called epitope spreading. Epitope spreading, and its absence in PV patients, is discussed on page 3890, 2nd column, 1st full paragraph of Veldman, which states as follows: "[o]ur findings suggests that intramolecular epitope spreading of Dsg3 T cell epitopes does not occur once the disease is clinically apparent since there was no direct relationship between Dsg3 peptide reactivity and a distinct clinical phenotype (*i.e.* active vs. remittent disease). Applicants respectfully submit that the sections of Veldman cited by in the Office Action fail to support a case of nonenablement.

(IV) The Office Action Fails to Consider the Required Eight Factors in Assessing Enablement

Applicants requested in the previous office action that if the Examiner maintained the enablement rejection, that the Examiner must consider the following eight factors:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The requirement to carefully consider each of these eight factors is clearly set forth in the MPEP 2164.01(a), which states as follows:

> [i]t is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of no enablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407.

The Office Action has again failed to consider, among others, the level of predictability in the art, the level of one of ordinary skill and or the state of the prior art (the Veldman reference cited by the Examiner does not predate the priority date of the subject application and therefore is not prior art). Applicants respectfully submit that absent the careful consideration of all eight factors as required by the MPEP that a prima facie case of nonenablement has not been made.

Based on the arguments set forth above, Applicants respectfully request reconsideration and withdrawal of the nonenablement ground of rejection.

Entering Amendment after Final

Applicants note that if entry of this amendment is not deemed by the Examiner to place the claims in immediate condition for allowance, it does place the claims in better condition for appeal according to MPEP 714.13(III), for example, by overcoming the objection to the Declaration. Accordingly, applicant respectfully requests that this amendment be entered.

CONCLUSIONS

Applicant believes no fee is due with this response under than the $225 fee for a two-month extension of time. However, if any additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. PEPT-P01-005 from which the undersigned is authorized to draw.

Dated: August 3, 2005

Respectfully submitted,

By _____

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